Delayed stroke after hospitalization for coronavirus disease 2019 pneumonia from common and internal carotid artery thrombosis

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ABSTRACT

Large vessel arterial thrombosis has been reported to complicate a subset of cases of coronavirus disease 2019 (COVID-19). Thrombosis of the extracranial carotid arterial system can lead to devastating stroke in some patients with COVID-19. We have presented the case of a patient previously hospitalized with COVID-19 for oxygen supplementation who had presented after discharge with delayed stroke from a right common carotid artery and internal carotid artery thrombosis. The thrombotic occlusion resolved with antithrombotic medications and no invasive intervention. The present report highlights the complicated and heterogeneous nature of COVID-19 and provides one approach to managing the devastating complication of stroke from carotid arterial thrombosis. (J Vasc Surg Cases and Innovative Techniques 2021;7:40-5.)

Keywords: Carotid artery; COVID-19; Stroke; Thromboembolism; Thrombosis

Among the many complications, stroke has been an increasingly reported complication of coronavirus disease 2019 (COVID-19).[1-16] The predisposing risk factors of COVID-19–associated stroke have remained unclear. In the present report, we have described the case of a patient previously hospitalized with moderately severe COVID-19, who had been readmitted with a delayed stroke from a common carotid artery (CCA) and internal carotid artery (ICA) thrombosis that was managed successfully with anticoagulation therapy. The patient provided written informed consent for the report of his case.

CASE REPORT

The patient is a 50-year-old male, former smoker, with a history of stage T3N0M0 laryngeal squamous cell carcinoma after total laryngectomy, partial pharyngectomy, laryngostomy, bilateral neck dissection, and placement of an anterolateral thigh free flap with 1 month of postoperative neck radiation 3 years before the acute stroke. He had a history of hypothyroidism, provoked pulmonary embolism after laryngectomy (not receiving anticoagulation therapy at the current presentation), and no known cardiac disease. A recent computed tomography angiogram at 9 months before the current presentation had demonstrated patent bilateral carotid arteries without stenosis (Fig 1), and no lymphadenopathy suggestive of cancer recurrence.

Eight days previously, the patient had been hospitalized at an outside hospital for 1 week of shortness of breath, cough, blood-tinged secretions, and subjective fevers and chills. At that presentation, he was febrile and mildly tachycardic but not in distress. He was diagnosed with polymerase chain reaction–confirmed COVID-19 pneumonia. His laboratory test results reflected chronic neutropenia and mild anemia (white blood cell count, 2.42 K/μL; hemoglobin, 12.4 g/dL) and new-onset thrombocytopenia (platelet count, 105 K/μL). He required 2 L of oxygen though his stoma for 5 days, and he had defervesced on hospital day 3. He received two doses of antibiotics, although his tracheal aspirate reflected only methicillin-resistant *Staphylococcus aureus* colonization. He was discharged after 6 days without supplemental oxygen.

Two days after discharge, he presented to our institution in sinus rhythm with mental status changes that evolved over several hours to left-sided flaccid paralysis and dysarthria. He was diagnosed with a right middle cerebral artery (MCA) territory stroke involving the insular cortex, frontal, parietal, and temporal lobes, with a minimal midline shift to the left (Fig 2). Ultrasonography and computed tomography angiography demonstrated extensive, nonocclusive acute thrombus in the right CCA and extending into the external carotid artery and ICA with reconstitution (Fig 3). Also, an acute nonocclusive thrombus was seen in the distal M1 segment of the right MCA (Fig 4).

His COVID-19 polymerase chain reaction assay was negative. The laboratory test results were as follows: D-dimer, 1600 ng/mL, hemoglobin A1c, 6.1%; thyroid-stimulating hormone, 5.6 mIU/L; triiodothyronine, 80 ng/dL; NS anticardiolipin IgM, 30 MPL. No hypercoagulability panel was performed. The findings from a two-dimensional transthoracic echocardiogram with agitated saline injection showed no thrombus, atrial septal defect, or right to left shunt. Heparin infusion and a high-dose

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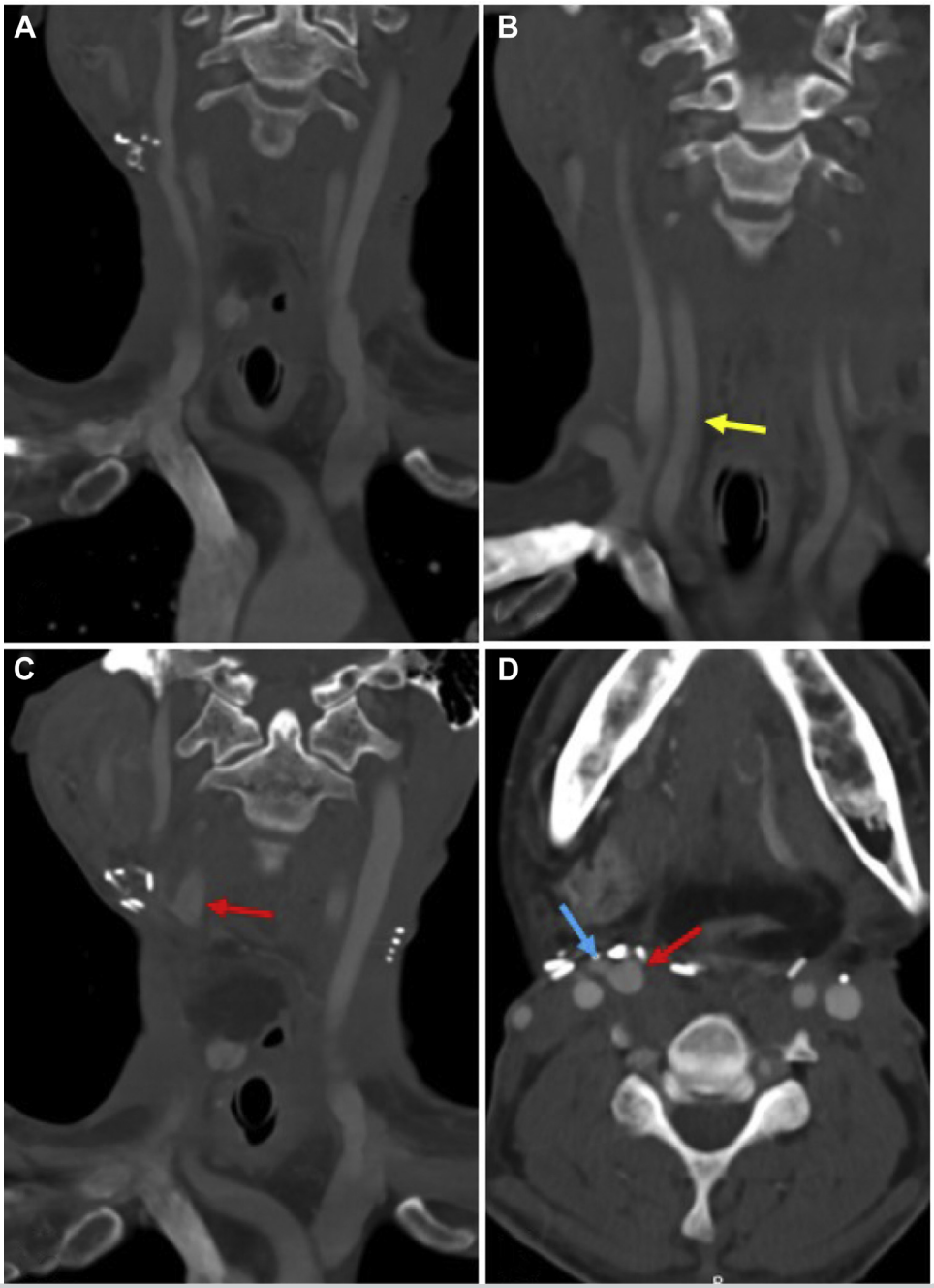

Fig 1. Previous computed tomography scan from an outside hospital 9 months previously, with evidence of a normal aortic arch **(A)** and patent carotid arterial system along the entire length **(B-D)**, including the common carotid artery (CCA; *yellow arrow*). **C** and **D,** Patent carotid bifurcation, with right internal carotid artery (ICA) and external carotid artery indicated by *red* and *blue arrows*, respectively.

statin was initiated for secondary stroke prevention. Antiplatelet therapy was withheld, owing to a concern for progression to malignant edema, which can require hemicraniectomy. He was not offered percutaneous thrombectomy or thrombolysis, because his symptoms had been present for >3 hours.

Vascular surgery was consulted 4 days after admission. The patient at the time was not receiving mechanical ventilation but was minimally responsive to sternal rub and demonstrated minimal motor function. Because of his mental status, it was difficult to determine whether his symptoms showed progression or stabilization. Continued noninvasive management was recommended. Repeat computed tomography angiogram 2 weeks after admission was performed to evaluate for progression and revealed near resolution of the right CCA, ICA, external carotid artery, and MCA thrombus (Fig 5).

During his hospitalization, the patient became increasingly responsive. He was discharged with full-dose apixaban and a high-dose statin after 2 weeks to a rehabilitation facility with a

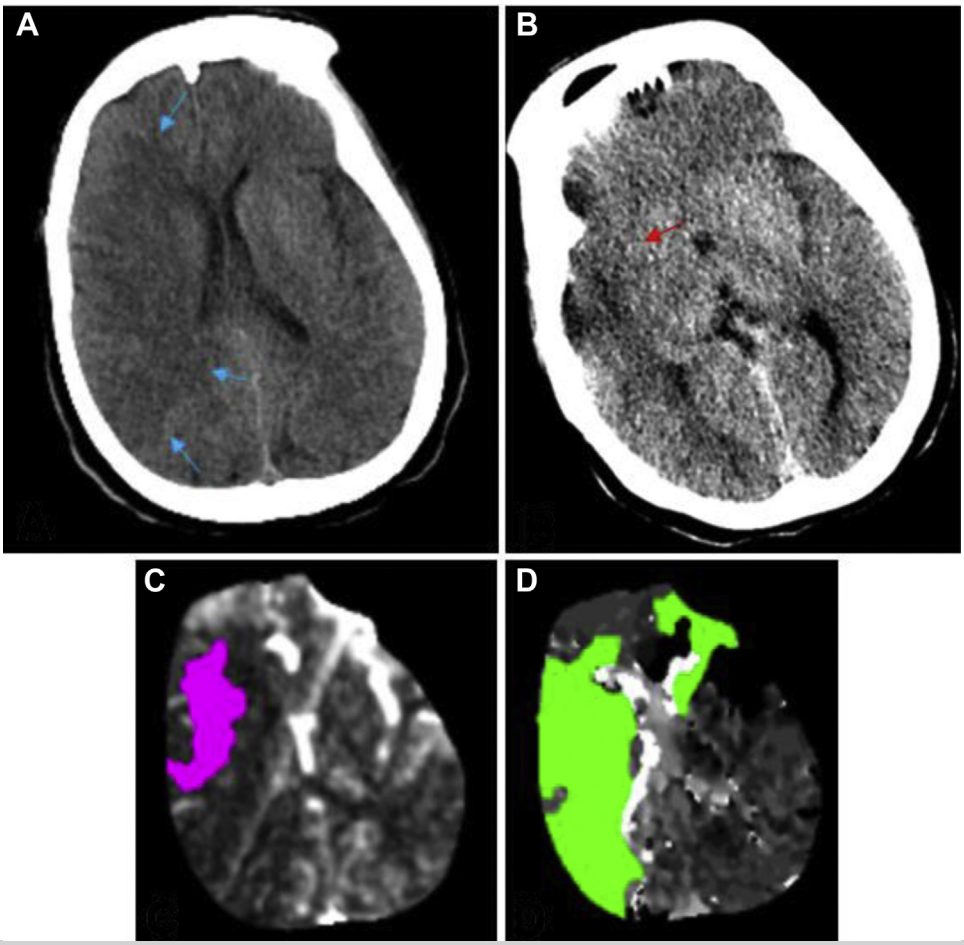

Fig 2. Computed tomography angiogram with perfusion imaging demonstrating right middle cerebral artery (MCA) territory stroke with large penumbra. **A** and **B,** Computed tomography scan of the brain showing loss of gray–white matter differentiation along the right MCA territory, including areas of frontal, parietal, and temporal lobes (*blue arrows*) and insular cortex (*red arrow*), suggestive of right MCA ischemic stroke. **C** and **D,** Perfusion map displaying cerebral blood flow <30% (*pink*) and time-to-peak concentration >6 seconds (*green*), representing predicted core infarct and potential penumbra, respectively.

modified Rankin scale score of 5, severely disabled, bedridden, incontinent, and requiring constant nursing care. He was discharged after 3 weeks of rehabilitation to home in the care of his family after improvement in his functionality, affect, and responsiveness. At the 3-month follow-up examination, the patient was weak on the left side but was ambulating, able to converse, and no longer requiring anticoagulation therapy. The 3-month carotid duplex ultrasound scan demonstrated no significant carotid stenosis bilaterally.

DISCUSSION

We have reported the case of a patient recently discharged and recovered from COVID-19, who had presented again nearly 2 weeks after the onset of his initial pneumonia symptoms with a stroke from a CCA and ICA thrombosis. Although the patient had a history of malignancy and radiation treatment, previous computed tomography scans as recently as 9 months before his readmission had demonstrated no significant atherosclerotic disease or radiation arteritis in his extracranial carotid system. His cancer had been in remission, with no concern for recurrence. The patient had no known coagulopathies, and his only previous thromboembolic event was a provoked pulmonary embolism. The aortic arch was free of significant atherosclerosis, and the echocardiography findings and persistent sinus rhythm did not suggest a cardiac embolism. Although it was not possible to prove a causative relationship, convincing evidence has shown that his event had resulted from COVID-19–induced hypercoagulability. Because of the delayed presentation, extensive thrombus, severity of the stroke, minimal recovery of function, and the risks associated with operative intervention in a radiated field, we elected for nonoperative management with anticoagulation therapy and a high-dose statin.

Several points are notable. First, the stroke occurred in a delayed fashion, presenting >1 week after his initial

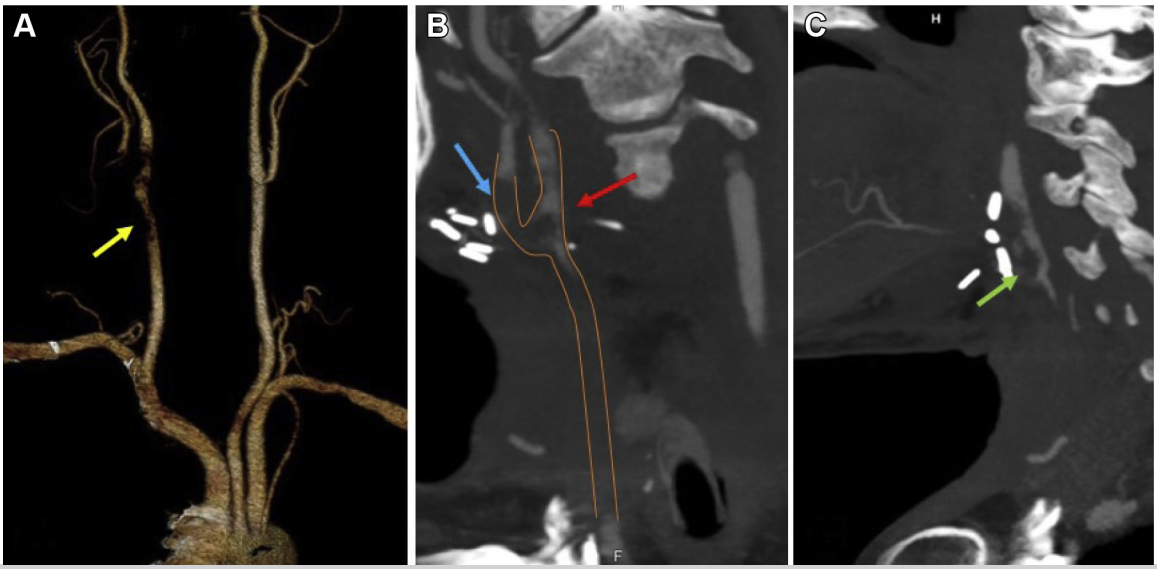

Fig 3. Three-dimensional reconstruction **(A)** and raw coronal **(B)** and sagittal **(C)** views of computed tomography angiogram, with evidence of extensive thrombus in the right common carotid artery (CCA; *yellow arrow*) extending to proximal internal carotid artery (ICA; *red arrow*) and external carotid artery (*blue arrow*). The *green arrow* identifies the carotid bifurcation.

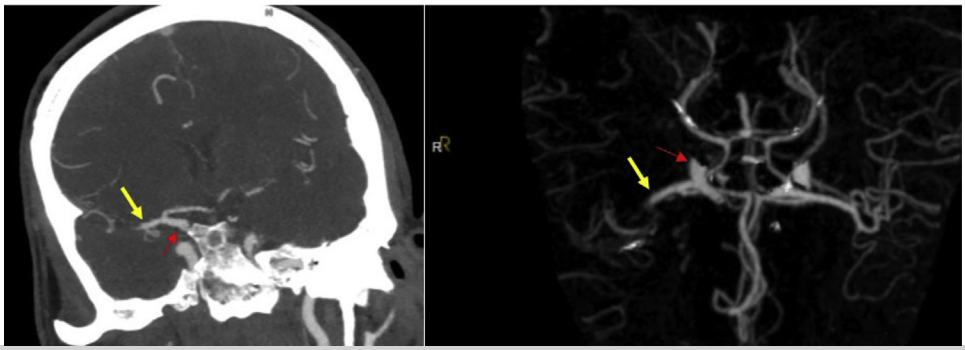

Fig 4. Computed tomography angiogram with perfusion demonstrating acute nonocclusive thrombus in the distal M1 segment of the right middle cerebral artery (MCA; *yellow arrow*). The *red arrow* identifies the right internal carotid artery (ICA).

hospitalization and >2 weeks after the onset of respiratory symptoms. Second, although the patient had required hospitalization initially for COVID-19 pneumonia, at no point was his condition critical. He had required only minimal noninvasive oxygen supplementation and was never admitted to an intensive care unit. The patient had not demonstrated hypotension, required pressor support, or demonstrated overt signs of sepsis to explain the thrombotic event. Third, although arterial thrombotic complications of COVID-19 have been increasingly reported in the literature, little is known about the risk factors underlying the events. Our patient had no evidence of active malignancy or previous carotid stenosis. However, it is likely that subclinical manifestations of his cancer and/or treatment had predisposed him to the occurrence of arterial thrombosis from COVID-19–induced coagulopathy. Finally, we have demonstrated near complete resolution of the thrombus within 2 weeks of the stroke with anticoagulation therapy. After completing a 3-month course of anticoagulation therapy, the findings from his carotid duplex ultrasound scan were essentially normal. Whether this can be attributable to the patient's native thrombolytic system or the pathophysiology of the COVID-19–induced hypercoagulability, or a combination of both, is unclear.

Increasing evidence has indicated that hypercoagulability is common among hospitalized COVID-19 patients.[12,17-23] To date, a few studies have reported identifying carotid artery thrombosis and stroke as a complication of COVID-19.[20,24] The earliest report from France identified a patient who, like our patient, had presented with stroke 7 days after his initial presentation

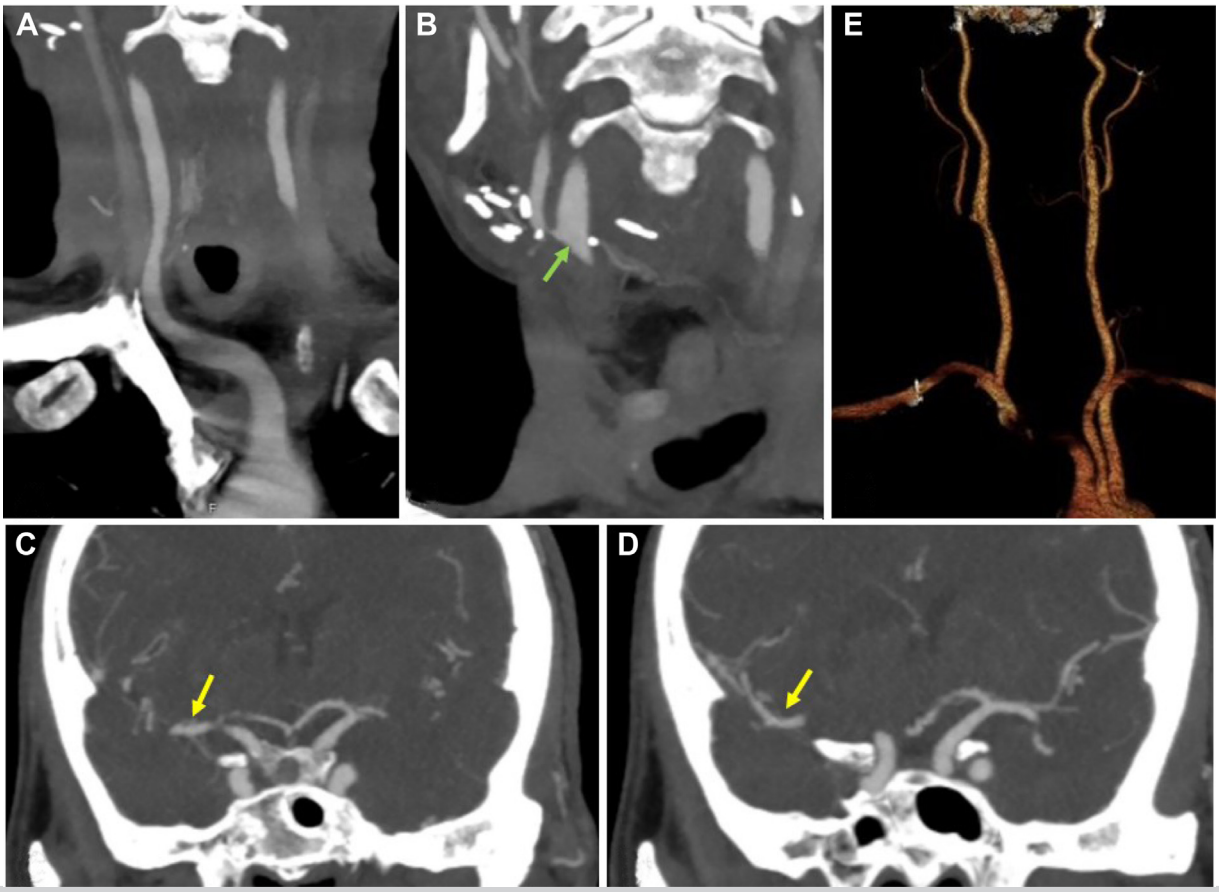

Fig 5. Follow-up computed tomography angiogram **(A-D)** and three-dimensional reconstruction **(E)** 2 weeks after the initial stroke presentation with evidence of decreased thrombotic burden and improved patency of the right carotid artery system and right middle cerebral artery (MCA; *yellow arrow*). The *green arrow* identifies a patent right carotid bifurcation. **C** and **D,** Images showing patency along a previously occluded distal M1 branch of the MCA.

to an emergency room with fever and dry cough.[22] No specific risk factors were identified in that patient, and the laboratory test results indicated inflammatory dysregulation but no hypercoagulability. Like our patient, the carotid thrombus had resolved with anticoagulation therapy and no invasive intervention. The largest series of carotid thrombotic complications resulting from COVID-19 identified six patients with carotid thrombosis and artery-to-artery embolism leading to stroke.[25] However, the typical vascular risk factors and plaque rupture from previous atherosclerosis from the proinflammatory state were thought to be the cause of the carotid thrombosis in that series.[25] Several of the patients had presented with only mild respiratory symptoms in that series, suggesting that the inflammatory and coagulopathic complications of COVID-19 might not directly correlate with the severity of the respiratory symptoms.

CONCLUSIONS

COVID-19 has been shown to be associated with a range of thromboembolic complications. A high degree of suspicion and the use of proper antithrombotic prophylaxis is critical. In select patients with arterial thrombotic complications, noninvasive management could be an effective treatment.

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